

CLAIMS

What is claimed is:

- Sub
a1
- 5 1. A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a to IgG1 upon *in vivo* administration to a mammal.
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2. The pharmaceutical composition of Claim 1 wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, CMV, HHV-6, HHV-7 or non-human equine herpesvirus type-1.
- 15 3. The pharmaceutical composition of Claim 2 wherein the herpesvirus is HSV-1 or HSV-2.
4. The pharmaceutical composition of Claim 3 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27.
- 20 5. A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to induce production of IFN- γ upon administration to a mammal.
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6. The pharmaceutical composition of Claim 5 wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.
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- See C2

7. The pharmaceutical composition of Claim 6 wherein the herpesvirus is HSV-1 or HSV-2.

8. The pharmaceutical composition of Claim 7 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27.

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Sub 9. A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a to IgG1 and induce an immunological protective effect upon administration to a mammal.

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15 10. A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said herpesvirus having an ability to effect an antibody subclass shift of IgG2a to IgG1 upon administration with the proviso that the herpesvirus is not Δ301, Δ504 or a gH deletion mutant.

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25 11. A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to induce production of IFN- γ upon administration to

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a mammal with the proviso that the herpesvirus is not d301, n504 or a gH deletion mutant.

Sub 3
5 12. A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a to IgG1 upon in vivo administration to said mammal.

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15 13. The method of Claim 12 wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.

14. The method of Claim 13 wherein the herpesvirus is HSV-1 or HSV-2.

15. The method of Claim 14 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27.

20 16. The method of Claims 12 wherein the mammal is in need of treatment for herpetic stromal keratitis.

Sub 4
25 17. A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect a

subclass shift of IgG2a to IgG1 and induce an immunological protective effect upon administration.

18. A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to induce production of IFN- γ upon administration.
19. The method of Claim 18 wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.
20. The method of Claim 19 wherein the herpesvirus is HSV-1 or HSV-2.
21. The method of Claim 20 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27.
- ~~22. The method of Claim 18 wherein the mammal is in need of treatment for herpetic stromal keratitis.~~
23. A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect a subclass shift of IgG2a to IgG1 upon administration

to a mammal with the proviso that the herpesvirus is not d301, n504 or a gH deletion mutant.

- 5 24. A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, 10 said mutant herpesvirus having an ability to induce production of IFN- γ upon administration with the proviso that the herpes virus is not d301, n504 or a gH deletion mutant.

- 15 25. A vaccine in a pharmaceutically acceptable carrier comprising a mutated herpesvirus capable of infecting a mammalian cell and of eliciting a protective immune response in a mammal vaccinated with said herpesvirus, said herpesvirus being characterized by a mutation in at least one gene encoding a protein essential for replication of said herpesvirus, said mutation rendering said virus replication-defective with the proviso that the herpesvirus is not a gH deletion mutant. 20

- 25 26. The vaccine of Claim 25, wherein said herpesvirus is HSV-1, HSV-2, VZV, EBV, HHV-6 or HHV-7.

27. The vaccine of Claim 25, wherein said protein is HSV-1 ICP27.

28. The vaccine of Claim 27, wherein said herpesvirus is n504R.

29. The vaccine of Claim 25, wherein said protein is HSV-1 or HSV-2 ~~LCP8~~.

30. The vaccine of Claim 29, wherein said herpesvirus is d301.

~~5 31. The vaccine of Claim 25, wherein said herpesvirus further encodes one or more heterologous genes.~~

32. A method of immunizing a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus capable of infecting a mammalian cell and of eliciting a protective immune response upon administration, said herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective.

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Adv.
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